

Crystal Structure of the Human Natural Killer Cell Inhibitory Receptor KIR2DL1 Bound to Its Class I MHC ligand

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Abstract No. Fan1001

Beamline(s): X25

Results: Inhibitory receptors on the surface of natural killer (NK) cells recognize specific MHC class I molecules on target cells and prevent the target cell lysis by NK cells¹. We have obtained crystals of the complex between the inhibitory NK receptor KIR2DL1 and its class I MHC ligand HLA-Cw4, which diffract to 2.8 Å resolution. A complete data set was collected with a Brandeis CCD detector at X25 beamline of the National Synchrotron Light Source, Brookhaven National Laboratory. The space group is C2, with unit cell parameters $a=213.63$ Å, $b=75.87$ Å, $c=125.75$ Å, $\alpha=\gamma=90^\circ$ and $\beta=120.962^\circ$. The complex structure has been determined by molecular replacement using the free KIR2DL1² and HLA-Cw4³ structures as search models. Each asymmetric unit contains one KIR2DL1 and two HLA-Cw4 molecules. KIR2DL1 forms a 1:1 complex with one HLA-Cw4 molecule while the other HLA-Cw4 provides lattice contacts. The structure has been refined at 2.8 Å resolution to a crystallographic R-value of 21.4% (R_{free}=25.6%). The interactions between KIR2DL1 and HLA-Cw4 are mainly mediated by complementary charges. Met 44 of KIR2DL1 lines an electronegatively charged pocket, which hosts the side chain of Lys 80 of HLA-Cw4 and confers KIR2DL1 its specificity for HLA-Cw4 related molecules.

References: 1. E. O. Long and N. Wagtmann, "Natural killer cell receptors," *Curr. Opin. Immunol.* 9, 344-350, 1997.

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3. Q. R. Fan and D. C. Wiley, "Structure of human leukocyte antigen (HLA)-Cw4, a ligand for the KIR2D natural killer cell inhibitory receptor," *J. Exp. Med.* 190, 113-123, 1999.